CNB Newsletter 11/2018

UNIVERSITÄT BERN

CLINICAL NEUROSCIENCE BERN

Dear CNB members,

With the CNB Newsletter, we intend to inform you about upcoming CNB events, ongoing projects and give insights to the research topics of selected CNB members.

We hope you enjoy reading the November 2018 edition.

Prof. Dr. Tobias Nef
President CNB

① Selected Research Groups

Dr. Jessica Peter

Cognitive functions and the Aging Brain
Department of Old Age Psychiatry and Psychotherapy

Declarative memory is the memory of facts and events, which can be consciously recalled (or declared), while non-declarative memory is the unconscious memory of skills; that is, how to do things (e.g., riding a bike). An important part of declarative memory is episodic memory, which represents our memory of experiences and specific events in time in a serial form, from which we can reconstruct the actual events that took place at any given point in our lives. Decline in episodic memory is one of the most common cognitive complaints among older adults, which is why our group focuses on the improvement of this type of memory through interventions.

We acquire episodic memories either intentionally or incidentally. During intentional learning, we are aware of the learning situation and we deliberately try to memorize. During incidental learning, on the other hand, learning is acquired 'on the way', that is, we 'pick up' information without having any intention to do so. In our experiments, we manipulate incidental learning by prompting individuals to solve a categorical decision task, in which they categorize stimuli according to certain rules, followed by an unexpected recall of those stimuli. According to the literature, a deeper analysis of those stimuli will lead to a more elaborate, longer lasting and stronger memory trace (and thus, better recall). A deeper analysis means that the individuals focus on the meaning of the stimuli rather than on their appearance. On the neuronal level, enhanced brain activity in the left dorsolateral Prefrontal Cortex (dlPFC) during processing of incidental learning tasks should lead to greater accuracy during subsequent recall and should draw attention to positive rather than to negative content, while increased activity in the right dlPFC should lead to an opposite effect. We currently test these hypotheses in healthy young individuals using non-invasive brain stimulation (which enables us to increase brain activity) and we will perform similar studies in healthy elderly people in the future.

Another important brain area for memory processes is the hippocampus, which is heavily affected by neuro-

degeneration in Alzheimer's disease (AD) and its precursor Mild Cognitive Impairment (MCI). The hippocampus is crucial for the formation of new memories as it links relevant information together and encodes it into a new memory by forming new synapses. Patients with MCI typically show enhanced activity in the hippocampus during memory tasks, accompanied with memory deficits, subsequent cognitive decline and a higher rate of progression to AD. Pharmacological treatment reduced this hyperactivity and thereby improved memory in MCI. Although one may expect that reducing brain activation in a given area will lead to a drop in performance, there is emerging evidence that hyperactivity in the hippocampus has a negative impact on cognition rather than a positive. Thus, reducing excess hippocampal activity seems to be a promising therapeutic target. However, pharmacological interventions have their disadvantages and limitations including side effects, reservations against medication, and non-response. An alternative and less harmful approach might be real-time functional MRI based neurofeedback. In this approach, participants are lying in the MR scanner while voluntarily controlling their brain activity in a given area. The training is accomplished by continuously measuring brain activity, analysing it in real-time, and then providing feedback about the current brain activity to the participant. With this exciting approach, we will both try to reduce hippocampal hyperactivity and improve memory functioning.

Besides remembering the past, memory serves another central function, namely plan for the future. This type of memory is referred to as prospective memory (PM) since it represents the ability to remember to perform an intention in the future. PM comprises multiple phases that rely on different cognitive processes. First, a person needs to form an intention (e.g., call a fried at six o'clock in the evening). During this intention-encoding phase, the person plans when (i.e., at six o'clock) and how (i.e., by phone) the intention will be performed. Then, the intention is stored in retrospective memory, while the person is engaged in other activities and might monitor for the PM target cue or target time, respectively. When the moment for completing the intention arises, the person has to retrieve the intended action, inhibit other ongoing activities, and switch to the intention as well as perform it as planned. Thus, PM is a challenge - especially in old age with increasing health-related PM demands. In our studies, we will investigate the influence of motivation on PM in elderly people and we want to explore the underlying neural mechanisms.

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Prof. Dr. med. Selma Aybek

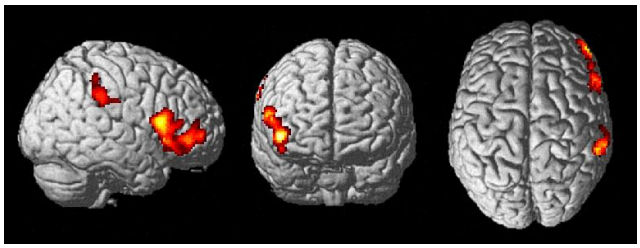
Functional Neurological Disorder (FND) Research Group
Department of Neurology, Inselspital

Functional neurological disorders (FND), formerly called Hysteria (by Hippocrates) and then Conversion Disorders (by Freud), represent a frequent disorder at the edge between Neurology and Psychiatry. Patients present with neurological symptoms (e.g., paralysis, tremor, convulsions) for which no neurological origin, such as stroke, tumour or epilepsy, is found. As FND represent the second most common reason for a neurology consultation, it is of utmost importance to better understand the mechanisms behind the development of the physical symptoms, in order to develop specific treatment plans. With the recent technological advances in neurosciences, several key studies have improved the understanding of FND. Recent evidence has suggested, for instance, an impairment in the sense of agency (the sense that we are the agents in control of our actions and sensation), as well as an abnormal processing of psychological stress, as key aspects in the appearance of the functional symptoms.

Our research focus is on the understanding of *how* and *why* the functional symptoms are produced in FND patients. We pursue the *how* stream by studying the neurobiological network of the sense of agency with functional magnetic resonance imaging (fMRI) and non-invasive brain stimulation techniques (e.g., transcranial magnetic stimulation – TMS). In particular, we investigate the role of the right temporo-parietal junction (rTPJ), a brain area known to show abnormal activation patterns in FND, in

agency processing, as well as the effects of TMS over the rTPJ on the sense of agency. Our main hypothesis is that the rTPJ is responsible for the detection of potential mismatches between sensory feedback from a motor action and the internal prediction of that action and, consequently, determines whether the motor outcome is self-generated (perfect match – positive agency), or not (mismatch – negative agency).

We pursue the *why* stream by studying the role of stress in FND. To this end, we treat our patients with Mindfulness-Based Stress Reduction (MBSR) therapy, a method that has already proved to reduce stress in other clinical populations, such as depression, chronic pain, and anxiety, and study its effects on standard biomarkers of stress (salivary cortisol and α-amylase). Our main hypothesis is that MBSR improves the functional symptoms, as well as the subjective perception of the symptoms themselves, by reducing stress levels in FND patients.



Preliminary results on the investigation of the network of agency. While healthy subjects play a computer-based game where the sense of control over the task is artificially reduced, the right temporo-parietal junction (rTPJ), a key area for agency processing, shows hyperactivity.

Our multidisciplinary team is composed by medical doctors, biomedical engineers, and neuropsychologists, joining their efforts in order to shed light on the neural mechanisms of FND. We are affiliated with the Department of Neurology (Inselspital), the University Institute for Diagnostic and Interventional Neuroradiology (Inselspital) and the University of Bern. We are supported by the Swiss National Foundation (SNF), the Leenaards Foundation, the Inselspital, and the University of Bern.

Selected publications:

- Identifying motor functional neurological disorder using resting-state functional connectivity. Wegrzyk J, Kebets V, Richiardi J, Galli S, Van de Ville D, Aybek S. NeuroImage: Clinical 2018;17:163-68.
- Biological and perceived stress in motor functional neurological disorders. Apazoglou K, Mazzola V, Wegrzyk J, Frasca Polara G, Aybek, S. Psychoneuroendocrinology Nov 2017;85:142-50.
- Increased methylation of the oxytocin receptor gene in motor functional neurological disorder: a preliminary study. Apazoglou K, Adouan W, Aubry J-M, Dayer A, Aybek S. Journal of Neurology, Neurosurgery & Psychiatry Sep 2017.
- The neural correlates of recall of life events in Conversion Disorder. Aybek S, Nicholson T, Zelaya F, O'Daly O, Craig T, David A, Kanaan R. JAMA Psychiatry. 2014. Jan 1;71(1):52-60.

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② Awards and Grants

Molly and Bernard Sanberg Memorial Award 2018

Award winner Hans Rudolf Widmer (left) during the Annual Conference of the ASNTR.

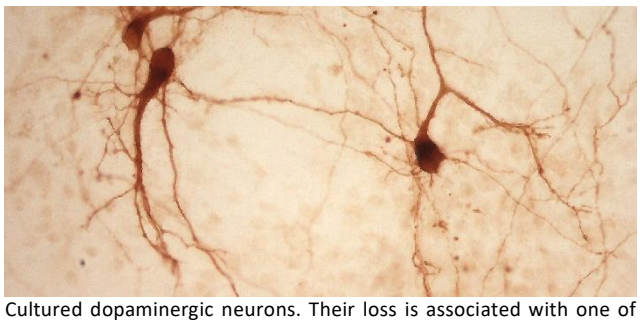
The Molly and Bernard Sanberg Memorial Award is presented periodically by the American Society for Neural Therapy and Repair (ASNTR) to an outstanding research contribution in the field of neural therapy and repair.

On occasion of the Annual Conference of the ASNTR, this year's Award was presented to Prof. Hans Rudolf Widmer in recognition of his research, which spans therapeutic strategies for neuropathological disorders, such as Parkinson's disease, to advancements in neuronal regeneration and cell transplantation. The official media release can be found here.

Hans Rudolf Widmer is the head of the Research Laboratory on Restorative Neurosurgery at the Department of Neurosurgery, Inselspital and member of the Cluster for Regenerative Neuroscience, DBMR. His research focuses on stem cell therapy for neurodegenerative diseases and neuropathological conditions. In line with this notion, he

is member of the Network for European CNS Transplantation and Restoration (NECTAR) and of the Research Committee Parkinson Schweiz. Since 2015 he serves on the editorial board of Cell Transplantation (section: Neuroscience and Tissue Engineering). Hans Rudolf Widmer organizes together with Prof. Volker Enzmann the Master course 'Disease & Repair in the CNS'. He is further a research group leader of the CNB Network.

We would like to congratulations Hans Rudolf on this great success!



Cultured dopaminergic neurons. Their loss is associated with one of the most prominent neurodegenerative disorders, Parkinson's disease.

③ Upcoming events

11. - 14. March 2019	Brainweek Bern 2019
12. March 2019	CNB Science Slam
14. June 2019	CNB Annual Meeting 2019

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